POLYMER-SILICA HYBRID PDOTS AND METHODS OF USE THEREOF

CROSS REFERENCES TO RELATED APPLICATIONS

[0001] This application is a Continuation of co-pending U.S. patent application Ser. No. 16/900,809, filed Jun. 12, 2019, which is a Continuation of U.S. patent application Ser. No. 16/309,795, filed Dec. 13, 2018, now U.S. Pat. No. 10,770,197, issued Sep. 8, 2020, which is a U.S. National Phase Application under 35 U.S.C. § 371 of International Patent Application No. PCT/US2017/037260, filed Jun. 13, 2017, now expired, which claims the benefit of U.S. Provisional Patent Application No. 62/350,126, filed Jun. 14, 2016, now expired, the disclosures of which are incorporated herein by reference in their entireties.

BACKGROUND

[0002] Advances in understanding biological systems have relied on applications of fluorescence microscopy, flow cytometry, versatile biological assays, and biosensors. These experimental approaches make extensive use of organic dye molecules as probes. But intrinsic limitations of these conventional dyes such as low absorptivity, and poor photostability have posed great difficulties in further developments of high-sensitivity imaging techniques and high-throughput assays. As a result, there has been considerable interest in developing brighter and more photostable fluorescent nanoparticles.

[0003] Traditional chromophoric polymer dots have been studied for imaging and detection techniques for researching chemical and biological analytes and systems. Functionalization of chromophoric polymer dots for use in bioconjugation has been attempted, but problems with polymer dot swelling, instability, and aggregation in biological buffer solutions, as well as nonspecific interactions in certain environments have been encountered.

SUMMARY

[0004] The present disclosure provides a new class of organic-inorganic hybrid polymer dots and related methods.

[0005] In various aspects, the present disclosure provides an organic-inorganic hybrid polymer dot comprising: a semiconducting chromophoric polymer; and an inorganic network, wherein the semiconducting chromophoric polymer and the inorganic network form an organic-inorganic interpenetrated network.

[0006] In various aspects, the present disclosure provides a method of making an organic-inorganic hybrid polymer dot, the method comprising: providing a solution, wherein the solution comprises a solvent, a semiconducting chromophoric polymer, and an organo-silane; and mixing the solution with an aqueous solution, wherein at least one of the solution or the aqueous solution comprises an organo-silane comprising X, wherein X is a functional group suitable for bioconjugation. Preferably or optionally, the solution can also comprise an additional silane that can help to make the hybrid polymer dot smaller and/or more compact.

[0007] In various aspects, the present disclosure provides an organic-inorganic interpenetrated hybrid chromophoric polymer dot comprising a semiconducting chromophoric polymer, an inorganic network, and a functional group that is suitable for bioconjugation.

[0008] In various aspects, the present disclosure provides an organic-inorganic hybrid polymer dot comprising: a semiconducting chromophoric polymer; X, wherein X is a functional group suitable for bioconjugation; and an inorganic network that is covalently bonded to the semiconducting chromophoric polymer.

[0009] This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the Detailed Description. This summary is not intended to identify key features of the claimed subject matter, nor is it intended to be used as an aid in determining the scope of the claimed subject matter.

INCORPORATION BY REFERENCE

[0010] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0012] FIG. **1** provides a schematic illustration of a method for preparing hybrid polymer dots.

[0013] FIG. **2** illustrates a method of preparing carboxylate functionalized PFBT hybrid polymer dots.

[0014] FIG. **3** illustrates Transmission Electron Microscopy (TEM) images of the hybrid polymer dots.

[0015] FIG. **4** illustrates comparative single particle fluorescence curves of bare PFBT polymer dots and the hybrid polymer dots prepared from PFBT, alkylsilane, and TEOS at different ratios.

[0016] FIG. **5** illustrates cellular labeling brightness for different hybrid polymer dot bioconjugates as well as bare polymer dot bioconjugates, as quantified by flow cytometry.

[0017] FIG. **6** shows fluorescence imaging of MCF cells specifically labeled with the hybrid polymer dot bioconjugates based on the blending set of PFBT/TMOS/TEOS.

[0018] FIG. **7** illustrates photostability of the MCF cells labeled with the hybrid polymer dot bioconjugates.

[0019] FIG. **8** shows fluorescence imaging of MCF cells specifically labeled with the hybrid polymer dot bioconjugates based on the blending set of PFBT/TCOS/TEOS.

[0020] FIG. **9** illustrates photostability curves of the MCF cells labeled with the hybrid polymer dot bioconjugates.

[0021] FIG. **10** illustrates results of gel electrophoresis of the hybrid polymer dots and related bioconjugates.

[0022] FIG. **11** shows flow cytometry results of MCF-7 cells labeled with the hybrid polymer dots.

[0023] FIG. **12** provides a general schematic illustration of conjugated polymers with a silane chain and functional silane chain for bioconjugation.

[0024] FIG. **13** provides a general schematic illustration of conjugated polymers with a silane chain and functional chain for bioconjugation.